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THE EFFECT OF CAFFEINE UPON BLOOD GLUCOSE LEVEL

J. Hankiewicz

Translation of "Wpływ stosowania kofeiny na poziom glikozy we krwi," Polski Tygod. Lekar. i Wiadomosci Lekar., Vol. 15, 1960, pp. 742-745

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16. Abstract

Caffeine, administered by different routes to normal and diabetic patients in 0.07-0.16 g doses, decreased blood glucose by 11.6 and 13.3 mg-%, respectively, after 30-5 min for parenteral or 45-50 min for oral administration. The effect was proportional to the dosage and was the greater the higher the initial hyperglycemia.

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THE EFFECT OF CAFFEINE UPON BLOOD GLUCOSE LEVEL

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Diabetic patients often drink genuine coffee to reduce /742* fatigue and the frequently associated "physical exhaustion symptoms." The general improvement in feeling observed after the drinking of coffee is related to circulatory changes in the system [2, 9, 11] caused primarily by the caffeine contained in the coffee [12, 13].

The pharmacology of caffeine is well-known; however, the mechanism of its biochemical effect still has not been explained conclusively. According to Hauschild [5], the most convincing view is that of Fröhlich and Zak [3]. In the opinion of these authors, caffeine increases the permeability of the cell membrane in the capillaries, and also the intracellular metabolism, which in turn leads to dilation of the vessels. Reduced permeability of the cell membrane is generally considered as one of the most pathogenic factors in diabetes, responsible for slowing down processes which break down the glucose in the cells and increase its level in the blood [1, 4, 6, 10]. If we assume that caffeine changes the permeability of the cell membrane not only in the endothelia of the blood vessels but also in other tissues, its role and effect on the system, especially among diabetic patients, will be seen in a new light which interests us. The idea in these assumptions is that caffeine, like insulin, will improve the efficiency of the glucose processes in the cells and thus reduce the glucose level in the blood.

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* Numbers in the margin indicate pagination in the foreign text.

I attempted to demonstrate the validity of these theoretical assumptions among patients, especially patients suffering from diabetes. An additional incentive for carrying out these studies was also the well-known observations that among people not used to genuine coffee, symptoms similar to those observed in moderate hyperglycemia occurred after the coffee was drunk (a tendency to perspire, "internal restlessness" and, sometimes, even tremors).

Observations and Method

Adult outpatients, whose blood sugar level was determined in the laboratory, were examined. Persons whose state of health made the use of caffeine inadvisable (persons with high blood pressure and persons sensitive to chemicals and medications) were excluded from the study. The caffeine was administered in three forms and doses: subcutaneous injection of caffeine sodium benzoate, manufactured by the Polish Pharmaceutical Plants (on the average, 0.08-0.1 g pure caffeine), orally, in the form of genuine coffee (from "Delicacies") in the amount of 5 g/100 ml boiling water (according to Walewski and Skrodzki [14], this corresponds to a 0.05-0.08 g caffeine dose), and in the form of a 5% aqueous pure caffeine solution (KHF packing) (0.15 g caffeine/30 ml).

A 0.1 ml blood sample was taken from the fingertip before the study and at the appropriate time after administration of the caffeine. According to Seyffert [11], caffeine administered orally, i.e. in the form of coffee or a solution, begins to have an effect after 10-20 min, and the strongest effect occurs after 1-2 hours. Obviously, this time is much shorter when the caffeine is injected. However, due to the outpatient character of the studies (the limited time of the patients), I was forced to take the second blood sample after a shorter time, namely 30-35 min after injection of the caffeine sodium benzoate and 45-50 min after oral administration of the coffee or caffeine solution. I

used the Hagedorn-Jensen method to determine the glucose level in the blood.

TABLE 1

	Number of persons examined	Including	
		Women	Men
Caffeine sodium benzoate	101	89	12
Genuine coffee	54	35	19
Caffeine solution	73	45	28
Total	228	169	59

In the cases that were observed, in addition to the glucose level in the blood, I took into account other factors such as the age of the patients, the duration of the disease, the method used to treat the diabetis (among diabetic patients), and also whether they drank or did not drink genuine coffee. These data enabled me to analyze the results of the study more thoroughly.

Results

Prior to the actual studies, I determined the glucose level in the blood 100 times from one sample. The mean error of measurement was (δ) = ±8 mg-%. To facilitate the study, the measurement error was taken as ±10 mg-% (this corresponds to 1.258), thanks to which the results could be evaluated more accurately [8]. The numerical values $X - X_0 = \pm X$, which, depending on the sign, corresponded to a decrease (-), increase (+), or no change (0) in the glucose level in the blood, were obtained from measurements of the differences in the glucose level after the administration of the caffeine (X) and before its administration (X_0). All patients were classified into groups. The glucose level /743

in the blood before caffeine administration was used as the basis for the classification. Group I included subjects in whom a normal glucose level was determined (healthy persons), group II, patients with severe hyperglycemia (above 300 mg-%), group III, patients with moderate hyperglycemia (200-300 mg-%), and group IV, persons with slight hyperglycemia (below 200 mg-%).

Discussion of Results

The decrease in the glucose level in the blood after administration of the caffeine was significant -- on the average, 12.1 mg-% among all persons studied (228 people), 11.6 mg-% among the healthy persons (52 people), and 13.3 mg-% among diabetic patients (176 people). The difference in the decrease in the level among healthy people and diabetic patients is not large when we consider the actual values without taking into account the age of the persons studied and the degree of hyperglycemia. A more pronounced change in the glucose level was detected among younger persons of whom, in my study, a large number was in the group of healthy persons. Among diabetic patients (Fig. 1), the decrease in the glucose level was most pronounced in the group of persons with hyperglycemia above 300 mg-% (30.7 mg-%) (i.e. about 10% of the original value), and smallest in the group with slight hyperglycemia (up to 200 mg-%), where it was 5.8 mg-% (about 2.5% of the original value). The correlation between the degree of glycemia and the reduced glucose level value obtained after administration of the caffeine was studied statistically (Table 2).

When all persons in whom the glucose level decreased after the administration of caffeine were taken into account (N = 111 persons examined), the statistical significance of the sample correlation coefficient r demonstrated that the reduction in the value depends on the degree of glycemia. On the other hand, the value of the regression coefficient b (for the

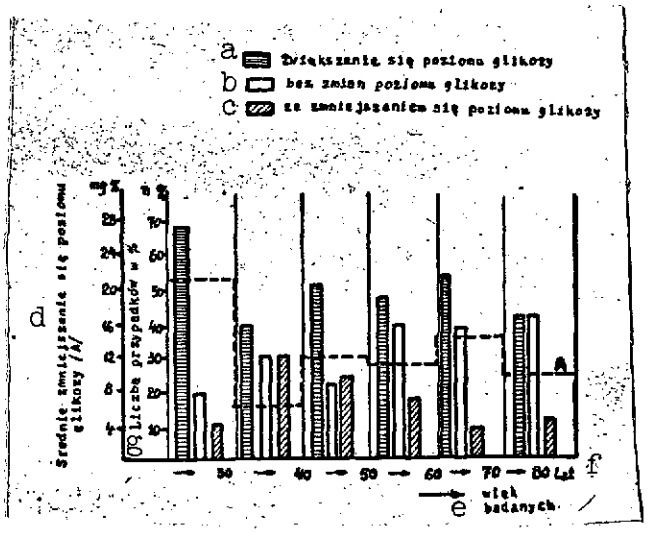

Fig. 1. Effect of caffeine administration on glucose level in blood vs. age of persons examined.

Key: a. Increase in glucose level; b. No change in glucose level; c. Decrease in glucose level; d. Mean decrease in glucose level [A]; e. Age of persons examined; f. Years; g. Number of cases (%)

particular methods used to administer the caffeine) shows that the most pronounced relationship occurred among persons who received the caffeine solution, in whom the reduction was, on the average, about 21 mg-% for every 100 mg-% of the original glucose level in the blood.

Similarly, the results pertaining to the number of cases are presented as mean values of the glucose level. Among 228 persons examined, a pronounced decrease in the glucose level after administration of caffeine was detected in 111 cases (49%), an increase in the level in 39 cases (17%), and, in the remaining 78 cases, the changes were within the range of measurement errors. Among 62 healthy persons, a decrease in the glucose level was detected in 24 persons (46%), an increase in six persons (12%), and no change in 22 persons (42%). Among the 176 diabetic patients, a pronounced decrease in the glucose level was detected in 87 cases (49%), a decrease in 33 cases (19%), and no change in the glucose level after caffeine administration in 56 cases (32%). The largest number of cases with a reduced glucose level was detected in the group of persons examined with hyperglycemia above 300 mg-% -- out of 33 persons examined, the glucose level decreased among 23 people (70%), increased among three people (9%), and did change among 7 people (21%). On the other hand, the smallest number of cases with a reduced glucose

TABLE 2

	N	(r)	Statistical significance level	(b)
Caffeine sodium benzoate	46	+0.83	>p = 99%	0.17
Caff Genuine coffee	21	+0.14	<p = 95%	--
Caffeine solution	44	+0.97	>p = 99%	00211
Total	111	+0.44	>p = 95%	00099

level was determined in the group of persons examined with hyperglycemia below and including 200 mg-% -- out of 56 persons examined, thebglucose level decreased after caffeine administration in 22 cases (39%), increased in 13 cases (23%), and didnnot change in 21 cases (38%).

A correlation, confirmed statistically, was detected between the glucose level and the caffeine dose (Fig. 2). The relationship between the caffeine dose and the decrease in the glucose level is statistically significant (for N = 111, r = 0.14, a t = 1.65). The highest hyperglycemia-reducing indicators were obtained after the administration of a 0.15 g caffeine dose in the form of an aqueous solution -- the mean decrease in the level was 20 mg-%, and with regard to the number of cases, out of 75 persons examined, a decrease was detected among 46 people (60%), an increase among 10 people (14%), and no changes among 19 people (20%) of the persons examined. On the other hand, the lowest hyperglycemia-reducing indicators were obtained after the administration of a 0.06 g caffeine dose in the form of genuine coffee -- out of a total number of 54 [sic] persons examined, the level was decreased on the average by 7 mg-% among 24 people (39%), increased among 24 people (38%), and no changes were detected among 23 (43%) of the persons examined. /744

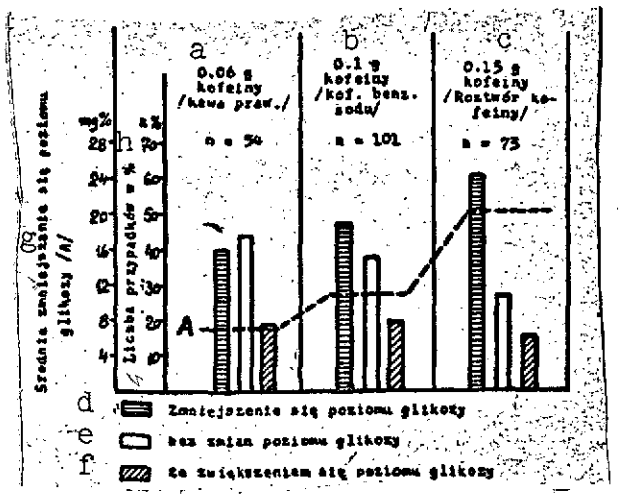

Fig. 2. Effect of caffeine administration on glucose level in blood. Relationship between caffeine dose and the form in which it is administered.

Key: a. 0.06 g caffeine (genuine coffee); b. 0.1 g caffeine sodium benzoate; c. 0.15 g caffeine (caffeine solution); d. decrease in glucose level; e. no changes in glucose level; f. increase in glucose level; g. mean decrease in glucose level; h. number of cases A (%)

In the analysis of the results, I also took into account the effect of such indirect factors as the duration of the disease among diabetic patients, and insulin therapy. One could make the assumption that protracted illness may intensify the disturbances in the carbohydrate exchange mechanism and thus delay the decrease in the glucose level in the blood under the influence of caffeine. It turned out that the duration of the disease had no effect on the results of the studies (Fig. 3).

I already mentioned in the introduction that, according to certain authors, caffeine and insulin have a similar effect. In this connection, one can assume that a system treated with insulin may "get used" to the mechanism which reduces the glucose level, so that the results will be different among people treated and not treated with insulin. This factor had no effect on the results in my studies (Fig. 4). Patients in whom the caffeine was injected subcutaneously showed small differences favoring those treated with insulin. In my opinion, this is due to the conditioned reflex formed undoubtedly in response to the subcutaneous injections in a certain group of patients treated with insulin.

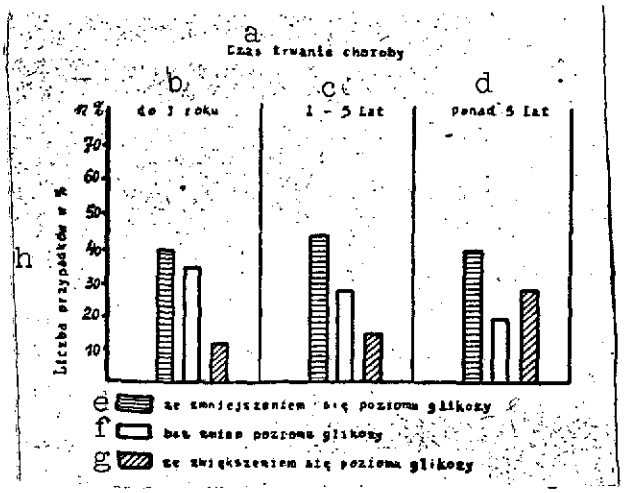

Fig. 3. Effect of caffeine administration on glucose level in blood vs. duration of diabetes.

Key: a. duration of illness; b. up to 3 years; c. 1-5 years; d. longer than 5 years; e. decrease in glucose level; f. no change in glucose level; g. increase in glucose level; h. number of cases (%)

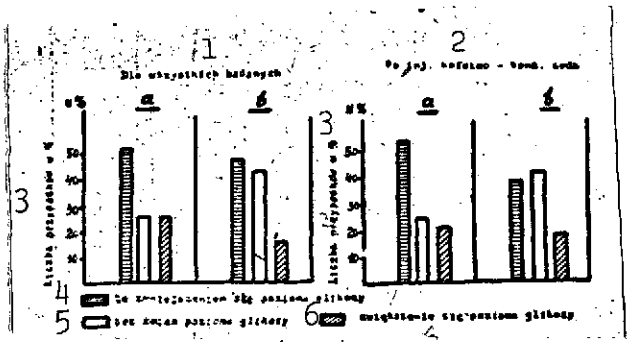

Fig. 4. Effect of caffeine administration on glucose level in blood among patients treated with insulin (a) and persons who did not receive insulin (b).

Key: 1. For all persons examined; 2. after injection of caffeine sodium benzoate; 3. 3. number of cases (%); 4. decrease in glucose level; 5. no changes in glucose level; 6. increase in glucose level

In the "coffee" group, an important factor in my studies was the genuine coffee drinking habit. The difference in the results among people who drink coffee frequently and infrequently is pronounced. The effect of the coffee is stronger among persons who drink it less frequently, Römpp [9] and Eichler [2].

Conclusions

It follows from the above studies that caffeine decreases the glucose level in the blood both among healthy persons with a normal glucose level and among diabetic patients with hyperglycemia. The hyperglycemia-reducing effect of caffeine depends not only on the form in which it is administered, but also on the dose -- the higher the pure caffeine dose, the more potent the effect.

The studies have shown that an intimate direct relationship exists between the glucose level in the blood and its reduction after the

administration of caffeine, i.e. the higher the glucose level in the person examined, the greater the hypoglycemia-reducing effect.

The administration of caffeine can be used as an adjoint method in the treatment of diabetes. In addition to the general improvement in the circulatory conditions, it may have a hypoglycemia-reducing effect, and thus act jointly with the insulin. Hence, th

Hence, the drinking of genuine coffee by diabetic patients is pharmacologically and biochemically sound, with the warning (which also follows from the above studies), that excessive drinking of genuine coffee weakens its hypoglyeemia-reducing effect.

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